PHARMACISTS' BULLETIN

NOVA SCOTIA SENIORS' PHARMACARE PROGRAM
PHARMACARE
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APRIL BULLETIN

CHOLINESTERASE INHIBITORS (ChEIs) - AN UPDATE ON UTILIZATION

Introduction and Background

Since July 1, 2003, the Nova Scotia Pharmacare Programs have covered three cholinesterase inhibitors (ChEIs) as exception status benefits: donepezil (Aricept®), galantamine (Reminyl® and Reminyl® ER) and rivastigmine (Exelon®).

An analysis of ChEI utilization in the Pharmacare Programs for the 23-month period from July 1, 2003 to May 27, 2005 is provided for your information.

During these 23 months, 2,371 beneficiaries were approved for coverage. This represents approximately 2.5% of the Nova Scotia Seniors' Pharmacare beneficiaries.

Patients switched to a second ChEI:
161 of the beneficiaries approved for coverage of a ChEI were subsequently approved to switch to a second ChEI. 49.7% of these beneficiaries switched due to gastrointestinal intolerance with the first ChEI. 25.5% switched due to target symptom deterioration with the first ChEI. The remaining 25% switched for a variety of reasons, which were largely side effect related.

ChEI Discontinuation:
By May 27, 2005, 699 beneficiaries (30%) appeared to have discontinued ChEI therapy. 47% discontinued during the first 90 day approval period; 69% discontinued by the end of the second 90 day approval period.

Costs:
Total expenditures for the ChEIs under the Pharmacare Programs is estimated to be $3 million in 2005/06. This includes government costs as well as beneficiary copayments.

Prescribers:
Requests for ChEI coverage were approved from 692 prescribers. 641 of these prescribers (92.7%) obtained approval for less than 10 beneficiaries, with the majority seeking coverage for only one or two beneficiaries.

# OF BENEFICIARIES APPROVED FOR COVERAGE	# OF PRESCRIBERS
55 +	3
20 to 40	11
10 to 16	37
9	15
8	17
7	17
6	29
5	44
4	72
3	85
2	122
1	239

Frequently Asked Questions

Pharmacare receives a number of questions related to the coverage criteria for the ChEIs. Included with this Bulletin are answers to the most frequently asked questions.

INCLUDED WITH THIS BULLETIN:

- **Frequently Asked Questions about Cholinesterase Inhibitors**
- **Cholinesterase Inhibitors Request Forms**

CRITERIA FOR COVERAGE OF DONEPEZIL, GALANTAMINE AND RIVASTIGMINE

For the treatment of mild to moderate probable Alzheimer's Disease or possible Alzheimer's Disease with vascular component, with Lewy bodies or other (as specified) who meet the following criteria:

Initiation of coverage in a ChEI-naive patient:
Coverage will be provided for an initial 90 days when all the following criteria are met:

- a Mini-Mental State Examination (MMSE) score of 10 to 30;
- a Functional Assessment Staging Tool (FAST) score of 4 or 5; and
- three target symptoms are established which will be monitored on an on-going basis to assist in determining clinical meaningfulness.

Continuation of coverage for a second 90-day period:
Coverage is extended an additional 90 days if:

- there is demonstrated stabilization or improvement in at least one target symptom during the initial 90 days of therapy.

Continuation of coverage for 6-month periods:
Coverage is continued in 6-month increments when:

- the information provided indicates the patient is in the mild to moderate stage of Alzheimer's Disease.
- a MMSE and FAST score must be provided 6 months after starting a ChEI and then only annually thereafter.

Initiation of coverage with a second ChEI for a patient who has previously taken no more than one other ChEI:
Coverage of a second ChEI is provided for an initial 90 days if:

- the reason for discontinuing the first ChEI is indicated; and
- any changes in target symptoms are indicated.

Coverage of a second ChEI is provided in the same manner as the first ChEI (i.e. 90-days, second 90-days, then continuation in 6-month periods if criteria are met).

Included with this Bulletin are the two request forms that can be used to request coverage:

- Request for 1st Cholinesterase Inhibitor (for initial 90 day coverage)
- Request to Switch to a 2nd Cholinesterase Inhibitor (for initial 90 days coverage)

These forms are also available at: *www.gov.ns.ca/health/pharmacare/alzheimer.htm*
No other forms are required as specialized request forms, which have been developed for each coverage period, will be automatically be sent to physicians to request continuation of therapy.

FREQUENTLY ASKED QUESTIONS ABOUT THE CHOLINESTERASE INHIBITORS (ChEIs)

1. **What is the objective of the criteria for coverage of the ChEIs?**

   The objective is to provide coverage for the ChEIs to patients who are in the mild to moderate stage of Alzheimer's Disease (AD) and are therefore most likely to benefit from them. At the same time, the criteria are intended to prevent the long term use of these drugs when they no longer make a difference in the life of a patient with AD.

2. **Where can I get a copy of the Reisberg Functional Assessment Staging Tool (FAST)?**

   Go to : *www.geriatric-resources.com/html/fast.html*

3. **Where can I get a copy of the standardized Mini-Mental State Examination (MMSE)?**

   Contact Pharmacare: Tel. (902) 496-7001 or 1-800-305-5026
   Fax (902) 465-9402

4. **Once I have a MMSE and FAST score for a patient, do I have to re-do them, or can I use the same scores on future forms?**

   Pharmacare requires a MMSE and FAST score at the time the ChEI is initially requested. Both tests must be repeated and the new scores submitted to Pharmacare to continue coverage after the initial 6 months. Thereafter, both tests must be repeated and the new scores sent to Pharmacare on a yearly basis. As a guideline, MMSE or FAST scores that are more than 2 months old should not be submitted to Pharmacare.

5. **When I use the Reisberg FAST to assess a patient, the patient sometimes scores a 6 because they have difficulty putting their clothes on properly or bathing without cueing. However, I still feel they are in the moderate stage of the disease and would benefit from a ChEI. What should I do?**

   The following table provides some general guidance for deciding if the FAST score is 4, 5 or 6 based on **instrumental activities of daily living (IADL)** and **basic activities of daily living (ADL)**.

	IADL	ADL
FAST Stage	managing money and meds, shopping, cooking, driving, housekeeping, using phone (Impairment of these activities requires some community or family support, but often the patient can be left alone for much of the day.)	feeding, toiletting, dressing, washing, mobility (Impairment of these activities leads to need for frequent personal nursing care.)
4	Needs assistance	Independent
5	Needs assistance or is dependent	Needs cueing or minimal assistance
6	Cannot do	Needs complete hands on assistance

Note: If there is a reason unrelated to dementia that a patient meets the criteria for a score of 6 on the Reisberg FAST scale, (i.e. they have urinary incontinence for some unrelated reason, or dressing difficulties due to arthritis), that criterion should be ignored when determining the patient's FAST stage.

6. Should I expect a patient's MMSE score to improve when they are taking a ChEI?

Response provided by Dr. Kenneth Rockwood, Professor of Medicine (Geriatric Medicine & Neurology) and the Kathryn Allen Weldon Professor of Alzheimer Research, Dalhousie University

The MMSE works very well as a screening test for cognitive impairment, but is less suited to detecting individual change. There are four reasons for this: the inter-rater and test-retest reliability are good, but not finely enough tuned to be certain that a 2-3 point difference might not just be due to measurement error. Secondly, there appear to be subtle learning effects, which are seen more with some patients than with others, so in this sense, it is biased. Third, the MMSE does not contain much by way of measurement of executive function (judgment, planning, initiative) and these areas are important; therefore, the MMSE is blind to important treatment effects, and thus biased in that way as well. Finally, even in areas in which it is not a bad measure (e.g. recent memory, language) the correlation between changes in those sub-measures of the MMSE and the attainment of clinically meaningful goals in those areas is very modest (in our experience, no more than 0.6). Each of these factors means the MMSE is not sufficiently sensitive to change for a clinician to rely on it alone.

This might raise the question of: Why do the MMSE at all? The MMSE offers the particular advantage that it allows for a systematic assessment of many aspects of cognitive function, which is preferable to relying solely on a clinical impression. Thus, the MMSE offers not just a number, but the merit of a systematic assessment which can make clinical judgments better.

7. Should I expect a patient's FAST score to decrease when they are taking a ChEI?

This response was also provided by Dr. Rockwood.

The FAST is a good example of an instrument that validly classifies people, but is less good at detecting change. It is uncommon for an individual to improve on the FAST.

8. I am told that target symptoms such as 'no longer able to drive' or 'decreased memory' are not good targets. What is wrong with these targets?

Target symptoms for each patient should be clinically important to that patient and their caregiver. They should also be measurable over time to determine whether they stabilize, improve, or deteriorate with therapy. How a target symptom responds to therapy is an important clue to whether the ChEI is really helping the patient. A target symptom such as 'no longer able to drive,' will not help in identifying how a patient is responding to the ChEI.

Sample measurable target symptoms in four different domains (cognition, function, behaviour and social/leisure) follow:

Cognition: The patient may have difficulty:

- Following a conversation with others
- Following a recipe or instructions
- Working the remote control (men)
- Dialing a phone (familiar number)
- Remembering children and or grandchildren's names
- Remembering important events of past week

Function: The patient may have difficulty:

- Doing own banking (machine or otherwise)
- Preparing a meal
- Grooming and dressing independently
- Bathing/showering independently
- Doing light house work independently
  (**OR** any Instrumental Activities of Daily Living)

Behaviour: The patient may:

- Be irritable more than once daily
- Have difficulty participating in daily conversations
- Have delusions or hallucinations
- Have fluctuations in memory impairment

Leisure/Social: The patient may have difficulty:

- Participating in past hobbies (e.g., card games, woodworking)
- Participating in social gatherings (e.g., hiding in a corner)
- Reading and enjoying a novel
- Enjoying gardening, watching T.V.
- Walking independently or taking dog for walk by self

9. Can I change a patient's target symptoms and if so, when is it appropriate?

This response was also provided by Dr. Rockwood.

You should change target symptoms whenever a new drug is being started. You should also review target symptoms annually, which is a useful time to see if they should be reset. Generally, valid target symptoms will hold for at least a year.

10. I find it difficult to discontinue a ChEI, even when a patient is clearly in the severe stage. Are there any reasons I can give the family, other than to save money for the patient and the Pharmacare Program?

This response was also provided by Dr. Rockwood.

The data for continuing a ChEI in severe dementia are not clear, and in general, there is no strong support for it. It is important to note that this also applies to most medications in severe dementia. For example, there are no data which would support anti-hypertensives or lipid lowering drugs in severe dementia. These should be reviewed as well. There are many people with severe dementia for whom the use of anti-hypertensives is likely to be harmful, as they will have orthostatic hypotension. Progressive autonomic failure is part of the natural history of most neurodegenerative dementias, so orthostatic hypotension is common. Discontinuing a ChEI should also be a prompt to review anti-hypertensives; unless they are being used symptomatically (e.g. for the treatment of angina) it is reasonable to consider slowly discontinuing them unless it can be shown that orthostatic hypotension is not present. The standard way to do this to is measure pulse and blood pressure: lying, standing and at two minutes.

11. Why doesn't Pharmacare cover Aricept 5mg tablets when I prescribe them twice daily?

This response was also provided by Dr. Rockwood.

There is no scientific rationale for using two 5mg doses instead of one 10mg dose. If a BID drug is felt to be desirable, two other ChEIs are available with BID dosing.

This portion of the response was provided by the Pharmacare Programs:

As indicated in the following table, all the ChEIs are "flat priced." Therefore, it is important to remember to change the tablet strength prescribed when increasing or decreasing dosages in order to minimize the daily drug cost. For example, using Aricept® 5mg tablets twice a day, instead of Aricept® 10mg daily, doubles the daily cost of treatment. The drug cost for a 30-day supply of Aricept® 5mg BID (60 tablets) is almost $300; while 30 Aricept® 10mg tablets would cost only about $150.

ChEI	Cost per tab, cap or mL (rounded off)
Aricept® 5mg tab	$4.98
Aricept® 10mg tab	$4.98
Aricept® 5mg tab UD	$4.98
Exelon® 1.5mg gelcaps	$2.63
Exelon® 3mg gelcaps	$2.63
Exelon® 4.5mg gelcaps	$2.63
Exelon® 6mg gelcaps	$2.63
Exelon® Oral Sol 2mg/mL	$1.40
Reminyl® ER 8mg caps	$4.98
Reminyl® ER 16mg caps	$4.98
Reminyl® ER 24mg caps	$4.98
Reminyl® 4mg tab	$2.68
Reminyl® 8mg tab	$2.68
Reminyl® 12mg tab	$2.68

*Prices obtained from McKesson Canada, Maritimes, November – January 2006.